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# The Toxicity of Some Organic Herbicides To Cattle, Sheep, and Chickens

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Washington, D.C.

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# The Toxicity of Some Organic Herbicides To Cattle, Sheep, and Chickens

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The Animal Disease and Parasite Research Division, Agricultural Research Service, has conducted studies on the toxicity of various organic herbicides to livestock for many years. Initial studies at Kerrville, Tex., for the most part involved long-term experiments with the more commonly applied chlorinated phenoxy acid compounds (12, 14).<sup>3</sup> Further studies with cattle and sheep have involved these and other organic herbicides. Results from some of these studies have been reported (6, 7, 8, 9, 10, 13).

Complementing all these studies have been additional reports that substantiate our own conclusions that a number of organic herbicides provide a comfortable margin of safety for cattle, sheep, and chickens when these herbicides are used according to directions (1, 2, 3, 4, 11, 15, 16, 19, 20).<sup>4</sup>

The studies at Kerrville were intensified, beginning in 1963; more cattle and sheep were studied, and chickens were added as experimental subjects. Usually these were short-term studies and were limited to 10, or fewer, consecutive daily doses. This would be a type of exposure that might be expected when these test animals consume relatively large quantities of the organic herbicides, either by carelessness or accident, for a short time. In some instances, however, sheep were exposed to as many as 481 consecutive daily doses.

The 29 organic herbicides chosen for our studies

were registered by the Pesticides Regulation Division of the Agricultural Research Service, at the time the studies were conducted. They were selected to allow as much diversification as possible, and correlated in considerable degree to the extent they were being used in agriculture. The herbicides in this report have been classified according to chemical similarity as follows: chlorophenoxy, amide, phenyl urea, thiocarbamate, triazine, benzoic acid, and miscellaneous compounds.

In this report poisoning was considered to have occurred when any observable sign of abnormal function or behavior was observed. In the mildest form of poisoning with most of the compounds, the signs were not spectacular. In many instances anorexia (lack or loss of appetite for feed—either partial or complete) was the only sign displayed. In these instances either the anorexia limited feed intake or the herbicide interfered with proper utilization of feed, or a combination of both could have affected the test animals. When such factor(s) resulted in either a 5-percent or more weight loss in cattle and sheep or a 5-percent or more decreased weight gain in chickens, it was considered significant. A few of the test animals died without previous signs of poisoning.

Cattle and sheep were routinely studied without parallel controls. Special tests that have been reported previously indicate that animals treated at less than toxic doses gained weight comparable with that of control animals (9, 21). The behavior and weight changes of cattle and sheep in these and other current studies and of animals in previous studies formed the basis for judging effect. In some measure the assessment of effect upon weight was therefore subjective rather than objective in cattle and sheep.

Chickens were studied with parallel controls and fed to make extensive weight gains. Because of the large numbers available, the assessment of effect upon weight gains could be objective.

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<sup>2</sup> Acknowledgment is made to personnel of the Crops Research and the Pesticides Regulation Divisions for their revisions and comments.

<sup>3</sup> Italic numbers in parentheses refer to Literature Cited, p. 26.

<sup>4</sup> Also McNamara, B. P. Summary of toxicity data on phenoxyacetates. 1967. [Personal correspondence.]



Weight gains or losses in chickens cannot be directly compared with the same changes in cattle and sheep because the latter were more mature and were being fed to maintain weight or

to gain slightly. Chickens were being fed to gain approximately 40 percent of their initial weight in the test period.

## INTERPRETATION OF HAZARD

To relate the toxic dosages found for cattle, sheep, and chickens to the application rates recommended for each herbicide (17, 18, 19), we calculated the probable amounts that could be consumed daily from recently sprayed fields or pastures. In these calculations, we considered neither the influence of environmental factors such as soil type, temperature, and rainfall, nor the decomposition rates of the herbicides being studied (5).

"The U.S.D.A. Summary of Registered Agricultural Pesticide Chemical Uses" was utilized for the application rates (17). An arbitrary, although realistic, yield of 0.1 pound of air-dry forage per square foot of area was selected, which is equivalent to approximately 2 tons per acre. This would represent a high-quality, improved pasture. The reader must, of course, make adjustments for local conditions. A sparse cover of vegetation would allow more of the herbicide to reach the ground and be unavailable to animals, whereas

a more lush vegetative cover would tend to hold more of the material available. In the latter case, however, less of the total forage of the area would be consumed in any one day.

Further assumptions were: (1) that an animal would consume, as forage, 3 percent of its body weight each day; and (2) that *all* the chemical formulation applied would adhere to the vegetation. Although this latter is never actually the case, this assumption gives the maximum exposure to be expected.

An application of 1 pound of chemical to 1 acre of land provides 10.4 milligrams for each square foot. We may simplify the whole calculation to a single statement that *1 pound actual of herbicide per acre provides a 7-milligram per kilogram (mg./kg.) dosage* to the animal under the conditions here assumed to exist. Each 2.2 pounds of animal weight equals 1 kilogram or 1,000 grams. In turn, 1 pound equals 454 grams. The equivalent of 1,000 mg./kg. is 454 milligram per pound (mg./lb.).

## EXPERIMENTAL ANIMALS

The cattle and sheep treated were obtained directly from local farmers and ranchers or through local auctions and were commercial stock. Cattle were of mixed breeding and sex, approximately 9 to 16 months old, and were classified as yearlings. Sheep were ewes and wethers of predominantly Delaine breeding. The cattle and sheep were maintained in open pens and were provided with rations of grain concentrates and hay. Mineral supplement and water were allowed as free choices.

The chickens were White Leghorns purchased from a commercial hatchery as day-old cockerels.

One trial, however, included 31 chickens of Cornish-White Rock breeding. All chickens were held in brooder or grower pens for 6 weeks, first on a commercial starting feed and later on a growing mash; then the trials were started. Before each experiment was started, each of the birds was weighed and legbanded, then placed with 4 others in isolated cages. All 5 were treated at the same dosage level of the organic herbicide. An additional 1 or 2 birds in each cage, also legbanded and weighed, served as controls.

## EXPERIMENTAL MATERIALS AND DOSAGES

The various organic herbicides utilized were usually commercially available formulations; however, exceptions were the use of: 2,4,5-T equivalent—pure acid or propylene glycol butyl ether ester—in 2 sheep in which residual effects were also studied (table 3); technical diphenamid in all trials (table 6); and, because of the unavailability of the commercial formulation, technical polychlorobicyclopentadiene isomers in a minority of cattle, sheep, and chickens more recently treated (table 25). Dosages were calculated on a mg./kg. basis for the active ingredient(s) of each chemical formulation to the body weight of the test animals. They were periodically recalculated in chronic studies as the weight of the animals changed.

Cattle and sheep were dosed with water-diluted formulation by use of a syringe, followed by a water rinse, or by use of a balling gun with the formulations in appropriate-sized gelatin capsules.

Chickens were dosed by water-diluted formulation by use of pipettes or by formulations in gelatin capsules. The treated chickens and the controls in

each cage were handled similarly; the controls were given untreated water or empty capsules.

The method used to select the number of doses administered and the dosage rates for each test animal involved several variables. The initial dosage rate was usually based on trial and error. When a toxic dosage was found, additional dosages above and below this rate were applied to other cattle, sheep, and chickens. Where a step-by-step increase of dosages indicated increased toxicity, repetition of individual dosages was not considered essential.

After each trial was completed, usually lasting 10 days or less, each surviving animal was weighed; the weight change was expressed as the percentage of initial, or preexposure, weight. Animals that died or were sacrificed during the course of the dosing or afterwards were examined by necropsy. Those sacrificed were moribund and death was considered imminent. Specimens for histopathological examination were collected for later study.

## RESULTS

### Chlorophenoxy Compounds

#### 2,4-Dichlorophenoxyacetic acid (2,4-D), alkanolamine salts (of the ethanol and isopropanol series)

Cattle and sheep were dosed by drench in all cases except one sheep, which was dosed by capsule (table 1). This sheep lost less weight comparatively (4 percent) at 250 mg./kg. after 10 doses than another (10 percent) at the same dosage by drench. Cattle were poisoned also at the 250 mg./kg., but after only 1. A sheep on a chronic study at 100 mg./kg. lost significant weight after 8. This loss was subsequently regained with no other apparent toxic effects in the following 473 doses. Chickens dosed at 250 or 500 mg./kg. 10 times by capsule had a significant reduced weight gain when compared with the controls.

All five cattle were treated on a 5-day per week regimen to arrive at the total doses received (6). The yearling dosed at 100 mg./kg. 86 times became tympanitic (distended with gas) and was

medicated for this condition. After 2 additional doses, this yearling was removed from the experiment because of rumen atony (lack of normal tone), and an uneventful recovery followed. One yearling treated at 250 mg./kg. one time developed dyspnea (difficult breathing) and other signs of respiratory difficulty with partial anorexia associated with swellings in the mandibular region. As a result of a later experiment discussed on page 5 of this report, we decided that the difficulty was probably caused by the irritation of the diluted formulation on the mucous membrane of the pharynx.

Signs of poisoning in cattle were anorexia, ataxia (failure of muscular coordination), and, in cases of prolonged exposure, ulceration of the oral mucous membranes. Signs in sheep were depression and weight loss.

At necropsy on 2 cattle and 1 sheep, lesions in the animals varied. Hemorrhages on the surface of the epicardium with excessive quantity of peri-



TABLE 1.—*Results of multiple dosing of cattle, sheep, and chickens with 2,4-dichlorophenoxyacetic acid (2,4-D), alkanolamine salts (of the ethanol and isopropanol series)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<i>Num-ber</i>			
Cattle:			
50-----	112	Drench---	NIE.
100-----	88	---do-----	Poisoned after 86 and survived.
200-----	44	---do-----	Poisoned after 25 and died. <sup>3</sup>
250-----	1	---do-----	Poisoned and survived. <sup>3</sup>
250-----	20	---do-----	Poisoned after 15 and died. <sup>3</sup>
Sheep:			
100-----	481	---do-----	11-percent weight loss after 8, otherwise NIE.
250-----	10	---do-----	10-percent weight loss.
250-----	10	Capsule--	4-percent weight loss.
500-----	7	Drench---	Poisoned and died.
Chickens: <sup>4</sup>			
100-----	10	Pipette---	36-percent weight gain.
250-----	10	---do-----	31-percent weight gain.
500-----	10	---do-----	Do.
Controls-----			38-percent weight gain.

<sup>1</sup> 2,4-Dow®, 65 percent emulsifiable concentrate, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

<sup>4</sup> Average results of 5 treated chickens.

cardial fluid were observed. Liver and kidneys were congested and friable and there was rumen stasis characterized by bright, undigested feed. The lungs were generally engorged with blood.

Application rates for 2,4-D salts range from 0.07 (1.12 ounces) to 40 pounds per land acre and to 87 pounds actual per water acre on submerged weeds. Application rates above 30 pounds actual per acre are hazardous for cattle, sheep, and chickens.

## 2,4-Dichlorophenoxyacetic acid (2,4-D), propylene glycol butyl ether ester

Either capsules or drenches were used for dosing cattle and sheep, capsules for chickens (table 2). Doses by capsule given a few animals resulted in

an apparently greater toxicity than by drench. A yearling and a sheep were poisoned at 250 mg./kg. by drench after 3 and 2 doses, respectively, with death resulting in only the sheep after 9. Doses by capsule caused poisoning and death at this dosage after 7 in cattle and 5 in sheep. One sheep had no ill effects at 100 mg./kg. by drench after 481. Chickens showed an average reduction in weight gain at 100 mg./kg. after 10.

Signs of toxicity in cattle and sheep were increasing depression and anorexia, followed by prostration until moribund. At necropsy the liver was soft and friable and the gall bladder was distended with bile. The kidneys were congested and friable and there were petechiae on the surface of the epicardium and large vessels. The lymph nodes in some animals were enlarged and hyperemic.

Application rates for 2,4-D esters range from 0.07 to 40 pounds actual per land acre and to 87 pounds actual per water acre on submerged weeds. Application rates above 30 pounds actual per acre are hazardous for cattle, sheep, and chickens.

TABLE 2.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,4-dichlorophenoxyacetic acid (2,4-D), propylene glycol butyl ether ester*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<i>Num-ber</i>			
Cattle:			
100-----	10	Drench---	NIE.
250-----	10	---do-----	Poisoned after 3 and survived, 12-percent weight loss.
250-----	7	Capsule--	Poisoned and died.
Sheep:			
100-----	481	Drench---	NIE.
250-----	9	---do-----	Poisoned after 2 and died.
250-----	5	Capsule--	Poisoned and died.
Chickens: <sup>3</sup>			
50-----	10	---do-----	49-percent weight gain.
100-----	10	---do-----	19-percent weight gain.
250-----	10	---do-----	Poisoned after 4, 13-percent weight loss.
Controls-----			41-percent weight gain.

<sup>1</sup> Esteron 99®, 38 percent emulsifiable concentrate, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.



### 2,4,5-Trichlorophenoxyacetic acid (2,4,5-T), propylene glycol butyl ether ester

Either capsules or drenches were used for dosing cattle and sheep, capsules for chickens (table 3). One yearling showed signs of poisoning at 250 mg./kg. after 4 doses by drench, whereas another at the same dosage had no ill effect after 10 by capsule. Although one sheep was poisoned at 100 mg./kg. by drench after 3 and died after 8, another had an initial weight loss at the same dosage by capsule but tolerated 367 before being poisoned and fatally affected. Chickens showed a significant decrease in average weight gain at 250 mg./kg.

Signs of poisoning in cattle and sheep were increasing anorexia and progressive weight loss, leading to weakness and prostration before death. At necropsy, the liver was swollen and often friable and the kidneys were congested. There were hemorrhages in the heart musculature. A general congestion of the visceral blood vessels was associated with rumen stasis characterized by bright undigested feed. Hyperemia and enlargement of the lymph nodes were noted in some animals. The two dead chickens showed congestion of the kidneys and intestinal mucosa.

Application rates for 2,4,5-T range from 0.5 to 4.5 pounds actual per acre. Such rates of this ester are not hazardous for cattle, sheep, or chickens.

### 2-(2,4,5-Trichlorophenoxy)propionic acid (silvex), propylene glycol butyl ether ester

Cattle were dosed either orally by drench or capsule or by rumen fistula, sheep were dosed by either drench or capsule, and chickens were dosed by pipette (table 4). Whereas 1 yearling showed no ill effects at 100 mg./kg. after 10 doses by capsule, another was poisoned after 19 by drench and died after 29. A sheep dosed at 50 mg./kg. by drench was poisoned and survived 10, but another dosed at 100 mg./kg. by capsule was poisoned after 9 and died after 11. In one study to determine the effect of silvex on various enzyme systems, 6 sheep were dosed at 100 mg./kg. by drench for 21 days, with no ill effects. The dosage was increased 50 percent to 150 mg./kg. for 10 days; 1 sheep died after 29, another after 31 (21). Chickens had a significant weight reduction after 10 at 100 mg./kg.

Signs of poisoning were only anorexia and weight loss in one sheep at 50 mg./kg., or anorexia with an increasing depressive state until recumbency in other poisoned sheep and cattle. Then a moribund condition developed, followed by death.

TABLE 3.—Results of multiple oral dosing of cattle, sheep, and chickens with 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), propylene glycol butyl ether ester<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
100-----	10	Drench---	NIE.
250-----	7	---do-----	Poisoned after 4 and died 2 days after last dose.
250-----	10	Capsule--	NIE.
<b>Sheep:</b>			
50-----	10	Drench---	Do.
100-----	369	Capsule--	9-percent weight loss after 8, poisoned after 367 and died.
100-----	8	Drench---	Poisoned after 3 and died.
250-----	7	---do-----	Do.
250-----	6	Capsule--	Poisoned after 4 and died.
250 <sup>3</sup> -----	4	---do-----	Poisoned and sacrificed.
250 <sup>4</sup> -----	4	---do-----	Do.
<b>Chickens:<sup>5</sup></b>			
100-----	10	---do-----	36-percent weight gain.
250-----	10	---do-----	18-percent weight gain.
500-----	10	---do-----	2 died after 5 and 9, 12-percent weight loss in survivors.
Controls-----			32-percent weight gain.

<sup>1</sup> Esteron 245 O.S.®, 65.3 percent emulsifiable concentrate, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> 2,4,5-T equivalent—pure acid.

<sup>4</sup> 2,4,5-T equivalent—pure ester.

<sup>5</sup> Average results of 5 treated chickens.

At necropsy, the liver was enlarged and friable and the kidneys were congested. There was an engorged rumen indicating stasis. A small abscess was found in the parotid lymph node in one yearling that developed a swelling in this region related to the chemical reaction associated with drenching. Other lymph nodes of the body were often enlarged and hemorrhagic.

Silvex administered in drench to cattle often caused an enlargement or swelling in the parotid and, in one instance, in the mandibular region. To determine whether this was the result of a systemic effect of silvex, we made a special study in which 6 yearlings were dosed at 50 mg./kg. (See table 4—

TABLE 4.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-(2,4,5-trichlorophenoxy)propionic acid (silvex), propylene glycol butyl ether ester*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
Cattle:	Num-ber		
25-----	73	Drench---	NIE, except for irritation effect after 20. <sup>3</sup>
50-----	73	---do----	NIE, except for irritation effect after 8. <sup>3</sup>
50-----	19	---do----	NIE, except for irritation effect after 19. <sup>3</sup>
50-----	27	---do----	NIE, except for irritation effect after 27. <sup>3</sup>
50-----	90	---do----	NIE.
50-----	56	Rumen fistula.	Poisoned and died. <sup>4</sup>
50-----	90	---do----	NIE.
50-----	90	---do----	Do.
100-----	29	Drench---	Poisoned after 19 and died after 29; irritation effect after 4. <sup>3</sup>
100-----	10	Capsule--	NIE.
Sheep:			
25-----	10	Drench---	Do.
50-----	10	---do----	Poisoned and survived, 15-percent weight loss.
100-----	11	Capsule--	Poisoned after 9 and died.
100-150 <sup>5</sup> --	29	Drench---	Poisoned after 28 and died.
100-150 <sup>5</sup> --	31	---do----	Poisoned after 30 and died.
100-150 <sup>5</sup> --	31	---do----	NIE.
100-150 <sup>5</sup> --	31	---do----	Do.
100-150 <sup>5</sup> --	31	---do----	Do.
100-150 <sup>5</sup> --	31	---do----	Do.
250-----	5	---do----	Poisoned and died.
Chickens: <sup>6</sup>			
50-----	10	Pipette---	48-percent weight gain.
100-----	10	---do----	25-percent weight gain.
250-----	10	---do----	28-percent weight loss.
Controls-----			41-percent weight gain.

<sup>1</sup> Kuron®, 46.5 percent emulsifiable concentrate, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in parotid or mandibular area enlargement accompanied by partial anorexia and and dyspnea.

<sup>4</sup> Mild localized infection developed in region of fistula.

<sup>5</sup> 21 doses at 100 mg./kg.; then 10 or fewer at 150 mg./kg.

<sup>6</sup> Average results of 5 treated chickens.

all yearlings dosed at 50 mg./kg. except the first listed.) Three of these were dosed by drench in the customary manner; 1 developed this parotid swelling after 19 and another after 27 doses. Rumen fistulas were prepared in the other 3 yearlings and silvex was introduced directly into the rumen. One of these yearlings died after 56, possibly influenced to some degree by a mild localized infection that developed in the region of the fistula. Three yearlings in this special study showed no ill effects from the dosage. We concluded that the enlargements were caused by the chemical reaction of the diluted herbicide formulation on the mucous membrane and underlying tissue of the pharyngeal region (9).

TABLE 5.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-methyl-4-chlorophenoxyacetic acid (MCPA), alkanolamine salts (of the ethanol and isopropanol series)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
Cattle:	Num-ber		
250-----	10	Drench---	NIE.
500-----	10	---do----	Poisoned after 8 and survived.
Sheep:			
50-----	10	Capsule--	NIE.
100-----	10	Drench---	Poisoned after 4 and survived, 17-percent weight loss.
100-----	383	Capsule--	Poisoned after 307 and died.
250-----	10	---do----	Poisoned and survived, 6-percent weight loss.
250-----	10	Drench---	Poisoned after 6 and survived, 6-percent weight loss.
500-----	10	---do----	NIE.
Chickens: <sup>3</sup>			
100-----	10	Capsule--	42-percent weight gain.
250-----	10	---do----	31-percent weight gain.
500-----	10	---do----	1 died after 1 dose; 20-percent weight loss in survivors.
Controls-----			41-percent weight gain.

<sup>1</sup> MCP Amine®, 69.1 percent emulsifiable concentrate, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.



Application rates for 2,4,5-TP (silvex) range from 0.13 (61 grams) to 8 pounds actual per acre, usually not more than 5. The higher rates would be no hazard to the three test species.

## 2-Methyl-4-chlorophenoxyacetic acid (MCPA), alkanolamine salts (of the ethanol and isopropanol series)

Cattle were dosed by drench, sheep by either drench or capsule, chickens by capsule (table 5). A yearling was poisoned at 500 mg./kg. after 8 doses, but the regimen was continued for a total of 10 with no further ill effects observed. Paradoxically, 2 sheep dosed at 250 mg./kg. were poisoned after 6 and 10, with a significant weight loss; whereas another showed no ill effects at 500 mg./kg. after 10. This difference in reaction could very likely be the result of individual tolerance. In a long-term trial 1 sheep dosed by capsule at

100 mg./kg., was poisoned after 307 and died after 383. In contrast, another sheep was poisoned at 100 mg./kg. after 4 by drench; it survived 10 but had significant weight loss. Chickens had significant reduced weights at 250 mg./kg.

Signs of poisoning of the sheep that died were anorexia, ataxia, muscular spasms, and dyspnea. The poisoned yearling became tympanitic and showed partial anorexia.

At necropsy on the sheep, the spleen was enlarged, lungs were congested, and kidneys were swollen and congested. There were hemorrhages on the surface of the epicardium and the liver was friable and light brown. The meningeal vessels were congested. At necropsy on the one chicken, the spleen was enlarged and there was redness of the intestinal mucosa.

Application rates for MCPA range from 0.13 to 2:10 pounds actual per acre, which would be no hazard to the three test species.

## Amide Compounds

### *N,N*-Dimethyl-2,2-diphenylacetamide (diphenamid)

All test animals were dosed by capsule (table 6). One yearling was poisoned at 250 mg./kg. after 3 doses and a sheep after 7. Chickens had a significant reduced weight gain at the same dosage.

The poisoned yearling developed an uncoordinated gait after 3 doses and further dosage was discontinued. The poisoned sheep developed lameness and muscular spasms after the 7th and final dose without forewarning signs. Anorexia, diarrhea, and prostration progressed until a moribund condition brought about the decision to sacrifice the sheep.

At necropsy, the ears of the sheep were congested. The subcutaneous tissues and areas delineating the different muscles were filled with yellow gelatinous material. There was rumen stasis characterized by bright undigested feed, the liver was enlarged and light brown, the kidneys were congested, the bladder contained brownish-tinged urine, and the adrenals were enlarged.

Application rates for diphenamid for weed control in various crops range from 3 to 6 pounds actual per acre. These rates would not be hazardous for the three test species.

### 2-Chloro-*N,N*-diallylacetamide (CDAA)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 7). The toxic

effect is evident at 25 mg./kg. in the 3 test species. One yearling was poisoned after 1 dose by drench, another after 2 by capsule, but each survived 10, with weight loss. One sheep was poisoned after 4 by capsule but survived 10, with weight loss,

TABLE 6.—Results of multiple oral dosing of cattle, sheep, and chickens with *N,N*-dimethyl-2,2-diphenylacetamide (diphenamid)<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<i>Cattle:</i>			
100-----	10	Capsule--	NIE.
250-----	3	---do----	Poisoned and survived, 8-percent weight loss.
<i>Sheep:</i>			
100-----	10	---do----	NIE.
250-----	7	---do----	Poisoned and sacrificed.
<i>Chickens:</i> <sup>3</sup>			
100-----	10	---do----	44-percent weight gain.
250-----	10	---do----	26-percent weight gain.
500-----	10	---do----	3-percent weight gain.
Controls-----			36-percent weight gain.

<sup>1</sup> Enide®, 100 percent technical powder, Upjohn Co., Kalamazoo, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

TABLE 7.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloro-N,N-diallylacetamide (CDAA)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
10-----	10	Drench---	NIE.
25-----	10	---do-----	Poisoned after 1 and survived, 6-percent weight loss.
25-----	10	Capsule--	Poisoned after 2 and survived, 7-percent weight loss.
50-----	1	Drench---	Poisoned and died.
<b>Sheep:</b>			
25-----	10	---do-----	NIE.
25-----	10	Capsule--	Poisoned after 4 and survived, 9-percent weight loss.
50-----	1	Drench---	Poisoned and died.
50-----	2	---do-----	Do.
50-----	5	Capsule--	Poisoned after 2 and died.
100-----	1	---do-----	Poisoned and died.
100-----	1	Drench---	Do.
250-----	1	---do-----	Do.
<b>Chickens:<sup>3</sup></b>			
10-----	10	Capsule--	46-percent weight gain.
25-----	10	---do-----	20-percent weight gain.
25-----	10	---do-----	39-percent weight gain.
50-----	10	---do-----	2 poisoned and died after 9, no weight change in survivors.
100-----	6	---do-----	All died after 1 to 6.
Controls-----			50-percent weight gain.

<sup>1</sup> Randox®, 47.1 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

whereas another showed no ill effect at the same dosage by drench. Chickens had significant reduced weight gains after 10.

Anorexia was the most prominent sign of poisoning. As additional doses were given to the cattle and sheep, there was increased salivation, and depression and prostration usually followed. Chickens were similarly affected by anorexia.

At necropsy on the yearling and the 6 sheep, the mucosa of the abomasum and small intestine was hemorrhagic. There was usually congestion of the lungs and the respiratory tract mucosa and the

kidneys were often enlarged and congested. Petechiae were noted on the surface of the bladder mucosa. Congestion of the intestinal mucosa was the most prominent lesion in chickens.

Application rates for CDAA range from 4 to 10 pounds actual per acre. These rates would be highly hazardous for all three test species.

## 2-Chloro-N,N-diallylacetamide (CDAA) and Trichlorobenzyl chloride (TCBC)

Dosing was done by drench to cattle, by capsule to chickens, and by either method to sheep. One yearling was poisoned at 50 mg./kg. after 2 doses

TABLE 8.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloro-N,N-diallylacetamide (CDAA) and trichlorobenzyl chloride (TCBC)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
25 <sup>3</sup> -----	10	Drench---	NIE.
50-----	10	---do-----	Poisoned after 2 and survived, 11-percent weight loss.
100-----	1	---do-----	Poisoned and died.
<b>Sheep:</b>			
25 <sup>3</sup> -----	10	---do-----	NIE.
25 <sup>3</sup> -----	10	Capsule--	Poisoned after 5 and survived, 11-percent weight loss.
50-----	10	Drench---	Poisoned after 2 and survived, 15-percent weight loss.
50-----	10	Capsule--	Do.
100-----	2	Drench---	Poisoned after 1 and died.
100-----	10	Capsule--	Poisoned after 2 and survived, 16-percent weight loss.
250-----	1	Drench---	Poisoned and died.
<b>Chickens:<sup>4</sup></b>			
37.5-----	10	Capsule--	43-percent weight gain.
75-----	10	---do-----	37-percent weight gain.
100-----	10	---do-----	24-percent weight gain.
100-----	10	---do-----	7-percent weight loss.
250-----	8	---do-----	All died after 1 to 8.
Controls-----			40-percent weight gain.

<sup>1</sup> Randox T®, 85.7 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo. (28.1 percent CDAA and 57.6 percent TCBC).

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> 25 mg./kg. is equivalent to 8.15 mg./kg. CDAA and 16.85 mg./kg. TCBC.

<sup>4</sup> Average results of 5 treated chickens.



but survived 10, with weight loss (table 8). One sheep was poisoned at 25 mg./kg. after 5 by capsule but survived 10 by drench, with weight loss; another sheep showed no ill effects at the same dosage administered by drench.

The only signs of toxicity were anorexia with loss of weight in poisoned cattle and sheep and reduced average gain or loss of weight in chickens. At necropsy on cattle and sheep, the abomasal and intestinal mucosa was hemorrhagic and the liver and kidneys were congested. In one animal,

the lungs were engorged with blood and there was blood-tinged froth in the respiratory tract. There were hemorrhages throughout the heart of the yearling that died after 1 dose at 100 mg./kg. At necropsy on chickens, kidneys were congested as was the intestinal mucosa.

Application rates for this combination of CDAA and TCBC range from 3.5 to 7 pounds actual per acre of corn. The 3.5-pound rate would be hazardous for sheep, and the 7-pound rate would be hazardous for cattle but not for chickens.

## Phenyl Urea Compounds

### 3-(*p*-Chlorophenyl)-1,1-dimethylurea (monuron)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 9). One yearling was poisoned but survived 1 dose at 500 mg./kg., which resulted in weight loss during the following 10-day period. Diarrhea resulted in cattle after 1 to 5 doses at 50, 100, and 250 mg./kg. by drench; however, diarrhea was not severe enough to result in significant weight loss or other related signs of poisoning. In contrast, another yearling dosed at 50 mg./kg. by capsule had no diarrhea or other ill effects after 10.

Sheep were poisoned and survived 100-mg./kg. dosages, with significant weight losses; however, the sheep dosed by capsule at this rate tolerated the formulation better than the 2 sheep dosed by drench. Although 2 sheep showed signs of poisoning after 4, only the sheep dosed by drench died after the additional doses. Chickens dosed at 25 mg./kg. had only reduced weight gains; chickens at 100 mg./kg. either died or lost weight after 8 to 10 doses.

The yearling poisoned at 500 mg./kg. became prostrate and was treated for tympanites. After 2 days it was ambulatory with an uncoordinated gait. One sheep dosed at 100 mg./kg. was poisoned and showed signs of excitability and an uncoordinated gait, which preceded prostration and severe weight loss; the 2d sheep dosed at this rate showed depression and anorexia; the 3d showed loss of equilibrium, which preceded prostration. Torticollis (twisted neck and unnatural position of the head) developed in this 3d sheep 2 days before death, which occurred 5 days after the 9th and last dose.

At necropsy, the lungs of the sheep were engorged with blood with accompanying congestion of the respiratory mucosa. The liver and kidneys were congested and enlarged. The meningeal vessels of the brain were engorged. Chickens

TABLE 9.—Results of multiple oral dosing of cattle, sheep, and chickens with 3-(*p*-chlorophenyl)-1,1-dimethylurea (monuron)<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
25-----	10	Drench---	NIE.
50-----	10	Capsule--	Do.
50-----	10	Drench---	Do.
100-----	10	---do----	Do.
250-----	10	---do----	Do.
500-----	1	---do----	Poisoned and survived, 11-percent weight loss.
<b>Sheep:</b>			
25-----	10	---do----	NIE.
50-----	10	---do----	Do.
100-----	4	---do----	Poisoned and survived, 19-percent weight loss.
100-----	10	Capsule--	Poisoned after 4 and survived, 15-percent weight loss.
100-----	9	Drench---	Poisoned after 4 and died, 20-percent weight loss.
250-----	2	---do----	Poisoned and sacrificed.
<b>Chickens:<sup>3</sup></b>			
10-----	10	Capsule--	54-percent weight gain.
25-----	10	---do----	33-percent weight gain.
50-----	10	---do----	20-percent weight gain.
100-----	10	---do----	1 poisoned and died after 8, 1-percent weight loss in survivors.
250-----	9	---do----	All died after 6 to 9.
Controls-----			47-percent weight gain.

<sup>1</sup> Telvar®, 80 percent wettable powder, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent; however, see narrative for results to cattle dosed by drench.

<sup>3</sup> Average results of 5 treated chickens.

generally showed congestion of the intestinal mucosa, with atrophied spleens.

Application rates for monuron generally range from 1.2 to 6.4 pounds actual per acre, although it may be used in water ditches at a rate equivalent to 80 pounds actual per acre. Rates in excess of 3 pounds per acre would be hazardous for chickens. A 6.4-pound rate would not be hazardous for cattle or sheep but the 80-pound rate would be highly hazardous for all three test species.

### 3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea (linuron)

Sheep were dosed by drench, chickens by capsule, cattle by either method. One yearling was poisoned at 50 mg./kg. by capsule after 10 doses, with a significant weight loss, whereas another yearling had no ill effects after 10 by drench (table 10). Sheep were poisoned at 50 mg./kg. after 1 or 8, with weight loss. Chickens dosed at 10 mg./kg. showed a significant reduced

TABLE 10.—*Results of multiple oral dosing of cattle, sheep, and chickens with 3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea (linuron)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
25-----	10	Drench...	NIE.
50-----	10	---do----	Do.
50-----	10	Capsule..	Poisoned and survived, 6-percent weight loss.
100-----	6	Drench...	Poisoned and died 2 days after last dose.
<b>Sheep:</b>			
25-----	10	---do----	NIE.
50-----	10	---do----	Poisoned after 1 and survived, 8-percent weight loss.
50-----	10	---do----	Poisoned after 8 and survived, 6-percent weight loss.
100-----	4	---do----	Poisoned and died.
250-----	3	---do----	Do.
<b>Chickens:<sup>3</sup></b>			
10-----	10	Capsule..	39-percent weight gain.
25-----	10	---do----	16-percent weight gain.
50-----	10	---do----	20-percent weight gain.
100-----	10	---do----	4 died after 8 or 9, 20-percent weight loss in survivor.
Controls-----			46-percent weight gain.

<sup>1</sup>Lorox®, 50 percent wettable powder, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

weight gain. No lesser dosage was tried. Four of 5 chickens in the 100-mg./kg. study group died after 8 or 9.

The most general signs of poisoning were anorexia and depression. Cattle had increased salivation and showed a marked weakness. All 4 poisoned sheep had an uncoordinated gait, and hematuria (discharge of blood in the urine) was observed in 2. Of these 2, one was poisoned at 50 mg./kg. after 8 doses and the other at 100 mg./kg. after 4 that preceded death.

At necropsy on cattle, there were congestion of the spleen and petechiae on the surface of the epicardium. In sheep there were hemorrhages on the muscle fasciae of the hindquarters and edema between the muscles. There were petechiae on the surface of the epicardium. The pericardial sac contained blood-tinged fluid. The lungs were engorged with blood and the respiratory mucosa was congested. There was marked congestion of the kidneys and petechiae were found on the surface of the bladder mucosa of both sheep. The liver was friable and swollen and there was congestion of the intestinal mucosa. At necropsy on chickens there were enlarged livers and congestion of the intestinal mucosa and kidneys.

The recommended application rates for linuron range from 1 to 3 pounds actual per acre either as a preemergent or a postemergent spray on crops. At these rates, there would be no hazard to cattle, sheep, or chickens.

### 3-Phenyl-1,1-dimethylurea (fenuron)

Cattle and sheep were dosed by drench, chickens by capsule (table 11). One sheep dosed at 100 mg./kg. was the most susceptible of all the test animals and was poisoned after 8 doses. Both cattle and chickens had ill effects only at 500 mg./kg. Cattle were poisoned by 2, whereas chickens showed decreased weight gains after 10.

Signs of poisoning in cattle and sheep were anorexia, depression, and ataxia. In the one yearling poisoned at 500 mg./kg., tympanites occurred. At necropsy on the sheep, there were hemorrhages on the surface of the epicardium, the lungs and liver were congested, and the liver was enlarged.

Fenuron is recommended for brush control in pastures and rangelands. As a spot treatment only, the application rate is 0.0156 pound (2 tablespoonfuls) of a 25-percent pelletized formulation per square foot. This rate could be a hazard to cattle, sheep, and chickens if a large area were to be treated.

### 3-(3,4-Dichlorophenyl)-1,1-dimethylurea (diuron)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 12). One



TABLE 11.—*Results of multiple oral dosing of cattle, sheep, and chickens with 3-phenyl-1,1-dimethylurea (fenuron)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
250-----	10	Drench---	NIE.
500-----	3	---do-----	Poisoned after 2 and survived, 20-percent weight loss.
<b>Sheep:</b>			
50-----	10	Capsule--	NIE.
100-----	10	Drench---	Poisoned after 8, with 9-percent weight loss after 10, died 8 days after last dose. <sup>3</sup>
250-----	10	---do-----	Poisoned and survived, 13-percent weight loss.
500-----	5	---do-----	Poisoned after 3 and sacrificed.
<b>Chickens:<sup>4</sup></b>			
250-----	10	Capsule--	47-percent weight gain.
500-----	10	---do-----	38-percent weight gain.
Controls-----			48-percent weight gain.

<sup>1</sup> Dybar®, 25 percent pellets, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Complications of pneumonia.

<sup>4</sup> Average results of 5 treated chickens.

yearling dosed at 100 mg./kg. by drench was poisoned; another dosed by capsule had no ill effects. One sheep dosed at 100 mg./kg. by drench was poisoned after 2 doses and had a significant weight loss during the next 8 days. Chickens dosed at 10 mg./kg. showed a significant decrease in weight gain. One chicken died at 100 mg./kg. after 10; the 4 surviving chickens showed weight loss.

Signs of poisoning in the yearling and the sheep were anorexia, depression, dyspnea, and prostration. In the 2 poisoned sheep, an uncoordinated gait was observed. Both sheep recovered after treatment was discontinued. At

necropsy on chickens, there was congestion of the intestinal mucosa and an enlarged, congested liver.

Application rates for diuron most commonly range from 0.2 to 9.6 pounds actual per acre. Rates in excess of 1 pound per acre would be hazardous for chickens. The 9.6-pound rate would not be hazardous for cattle and sheep. A rate of 80 pounds actual per acre is used in irrigation ditches and would be highly hazardous for all three test species.

TABLE 12.—*Results of multiple oral dosing of cattle, sheep, and chickens with 3-(3,4-dichlorophenyl)-1,1-dimethylurea (diuron)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
50-----	10	Drench---	NIE.
100-----	10	---do-----	Poisoned and survived, 9-percent weight loss.
100-----	10	Capsule--	NIE.
<b>Sheep:</b>			
25-----	10	Drench---	Do.
50-----	10	Capsule--	Do.
50-----	10	Drench---	Do.
50-----	10	---do-----	Do.
100-----	2	---do-----	Poisoned and survived, 12-percent weight loss.
250-----	1	---do-----	Poisoned and survived, 8-percent weight loss.
<b>Chickens:<sup>3</sup></b>			
5-----	10	Capsule--	58-percent weight gain.
10-----	10	---do-----	37-percent weight gain.
25-----	10	---do-----	37-percent weight gain.
50-----	10	---do-----	14-percent weight gain.
100-----	10	---do-----	1 poisoned and died after 10, 17-percent weight loss in survivors.
250-----	9	---do-----	All died after 8 or 9.
Controls-----			50-percent weight gain.

<sup>1</sup> Karmex®, 80 percent wettable powder, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

## Thiocarbamate Compounds

### S-2,3-Dichloroallyl diisopropylthiocarbamate (diallate)

Cattle and sheep were dosed by either capsule or drench, chickens by capsule (table 13). The toxic dosage was 25 mg./kg. for cattle and sheep.

One yearling was poisoned after 1 dose by drench; another was poisoned after 5 by capsule. In comparison, 1 sheep dosed at this rate was poisoned after 5 doses by drench; another was poisoned after 1 by capsule. One sheep dosed at 25 mg./kg. had no ill effect from 10 by drench;

whereas the other 2 sheep dosed at this rate, 1 by drench and 1 by capsule, were poisoned. This, presumably, would be due to individual tolerance. Chickens dosed at 125 mg./kg. or higher had significant reduction in weight gain.

Signs of poisoning in cattle and sheep were muscular spasms, ataxia, and depression, generally followed by prostration. A delayed alopecic effect (loss of hair or wool—either partial or complete) was seen in the more chronically affected animals, at times 60 days after dosing was discontinued. The most prominent sign of poisoning in chickens was anorexia, resulting in decreasing weight gains, weight loss, or death.

At necropsy on cattle and sheep, gross lesions consisted of a congested and friable liver, congestion of the kidneys with petechiae on the surface of the bladder mucosa, and, in one sheep, blood-engorged lungs and hemorrhagic intestinal mucosa. At necropsy on chickens, the kidneys were congested, the liver was swollen, and the intestinal mucosa was hemorrhagic.

Application rates for diallate range from 1.25 to 2 pounds actual per acre, which would not be hazardous for the three test species. However, only a modest increase to 3 pounds actual per acre would be hazardous for cattle and sheep.

### S-2,3,3-Trichloroallyl diisopropylthiocarbamate (triallate)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 14). A yearling was poisoned at 25 mg./kg. after 5 doses by drench but survived 5 additional doses, with significant weight loss. One sheep was poisoned at 50 mg./kg. after 2 by capsule, but survived 8 additional doses, with severe weight loss. In contrast, 2 sheep dosed at 50 mg./kg. by drench had no ill effects after 10 and 60 consecutive doses. Chickens dosed at 175 mg./kg. had a significant reduction in average weight gains.

Signs of poisoning in cattle and sheep were anorexia and subsequent large percentages of weight loss. A long recuperative period usually followed toxicosis. Muscular spasms, diarrhea, and ataxia were seen in a poisoned sheep that recovered. At dosages over 100 mg./kg., chickens had anorexia, resulting in reduced weight gains. All chickens were fatally affected at 250 mg./kg., showing congestion of the liver and kidneys and hemorrhagic intestinal mucosa at necropsy.

Application rates for triallate range from 1 to 1.25 pounds actual per acre. At such rates it would not be a hazard to the three test species.

TABLE 13.—Results of multiple oral dosing of cattle, sheep, and chickens with S-2,3-dichloroallyl diisopropylthiocarbamate (diallate)<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>	Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
Cattle:	Num-ber			Sheep—Con:	Num-ber		
10-----	10	Drench---	NIE.	25-----	19	Capsule--	Poisoned after 1 and survived, 20-percent weight loss, partial alopecia.
25-----	2	---do-----	Poisoned after 1 and survived, 5-percent weight loss.	50-----	8	Drench---	Poisoned after 3 and sacrificed.
25-----	10	Capsule--	Poisoned after 5 and survived, alopecia of the tail 60 days after last dose, 17-percent weight loss.	100-----	3	---do-----	Poisoned and survived, complete alopecia within 21 days after last dose, 14-percent weight loss.
50-----	8	---do-----	Poisoned after 7 and survived, alopecia of the tail 60 days after last dose, 11-percent weight loss.	250-----	2	---do-----	Poisoned after 1 and died.
50-----	6	Drench---	Poisoned after 3 and survived, 20-percent weight loss.	Chickens: <sup>3</sup>			
Sheep:				50-----	10	Capsule--	64-percent weight gain.
25-----	10	---do-----	NIE.	100-----	10	---do-----	51-percent weight gain.
25-----	10	---do-----	Poisoned after 5 and survived, 7-percent weight loss.	125-----	10	---do-----	36-percent weight gain.
				150-----	10	---do-----	22-percent weight gain.
				175-----	10	---do-----	9-percent weight loss.
				250-----	10	---do-----	All died after 7 to 10.
				Controls-----			55-percent weight gain.

<sup>1</sup> Avadex®, 45.7 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo.

<sup>2</sup> NIE indicates no apparent ill effects.

<sup>3</sup> Average results of 5 treated chickens.



TABLE 14.—*Results of multiple oral dosing of cattle, sheep, and chickens with S-2,3,3-trichloroallyl diisopropylthiocarbamate (triallate)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>	Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
Cattle:	Num-ber			Sheep—Con:	Num-ber		
10-----	10	Drench---	NIE.	100-----	10	Drench---	Poisoned after 1 and survived, 21-percent weight loss.
25-----	10	---do-----	Poisoned after 5 and survived, 5-percent weight loss, long recuperative period.	100-----	4	---do-----	Poisoned and survived, 20-percent weight loss.
50-----	10	Capsule--	Poisoned after 4 and survived, 12-percent weight loss.	250-----	2	---do-----	Poisoned and survived, 11-percent weight loss.
50-----	10	Drench---	Poisoned after 3 and survived, 16-percent weight loss.	Chickens: <sup>3</sup>			
Sheep:				50-----	10	---do-----	59-percent weight gain.
25-----	10	---do-----	NIE.	100-----	10	---do-----	55-percent weight gain.
50-----	10	---do-----	Do.	175-----	10	---do-----	10-percent weight gain.
50-----	60	---do-----	Do.	200-----	10	---do-----	17-percent weight gain.
50-----	10	Capsule--	Poisoned after 2 and survived, 18-percent weight loss.	250-----	10	---do-----	All died after 7 to 10.
				Controls-----			41-percent weight gain.

<sup>1</sup>Avadex BW®, 46.3 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo.

<sup>2</sup>NIE indicates no ill effects apparent.

<sup>3</sup>Average results of 5 treated chickens.

## Triazine Compounds

### 2-Chloro-4-ethylamino-6-isopropylamino-s-triazine (atrazine)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 15). The toxic dosage for cattle was 25 mg./kg. after 8 doses by drench and 2 by capsule. The toxic dosage for sheep was 5 mg./kg. No lesser dosage was tried. However, one sheep received 199 consecutive doses at 50 mg./kg. before it was poisoned and died. Chickens given 10 at 50 mg./kg. had a significant reduction in weight gains.

Signs of poisoning in cattle and sheep were muscular spasms of varying intensity in the hind quarters, a stilted gait and stance, and anorexia. In 2 sheep dosed at 100 mg./kg., when dosing was continued after moderate signs of poisoning developed, apparent improvement was observed until unexpected death occurred after 8 and 10 doses.

At necropsy, lesions of the yearling and the sheep varied somewhat. Petechiae on the surface of the epicardium and congestion of the kidneys, liver, and lungs were generally present. On occasion, the liver was light brown and friable. Some, but not all, of the dead animals had enlarged adrenals, as reported previously (10).

Application rates for atrazine range from 0.4 to 6.4 pounds actual per acre. Rates of less than 1 pound would be hazardous for sheep. Rates of 3 pounds actual per acre would be hazardous for cattle. The 6.4-pound rate would be hazardous for chickens.

### 2-Chloro-4,6-bis(ethylamino)-s-triazine (simazine)

Cattle were dosed by drench, chickens by capsule, and sheep by either drench or capsule (table 16). Two yearlings were poisoned at a dosage of 25 mg./kg. after 3 and 10 doses. One sheep was poisoned at 50 mg./kg. after 17 and died after 31, whereas another was poisoned after 10 and survived with an 18-percent weight loss. Chickens dosed at 50 mg./kg. 10 times showed a reduced weight gain.

Signs of poisoning in cattle and sheep were anorexia, depression, muscular spasms, and dyspnea of increasing intensity. Weakness and an uncoordinated gait were commonly observed in severely poisoned animals.

At necropsy, lesions in cattle and sheep generally were congestion of the lungs and kidneys;

TABLE 15.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloro-4-ethylamino-6-isopropylamino-s-triazine (atrazine)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
10-----	10	Drench---	NIE.
25-----	10	---do-----	Poisoned after 8 and survived, 13-percent weight loss.
25-----	10	Capsule--	Poisoned after 2 and survived, 13-percent weight loss.
50-----	9	---do-----	Poisoned after 1 and survived, 19-percent weight loss.
100-----	1	---do-----	Poisoned and survived.
250-----	2	Drench---	Poisoned after 1 and died.
<b>Sheep:</b>			
5-----	10	---do-----	Poisoned and survived, 13-percent weight loss.
10-----	10	---do-----	Poisoned after 8 and survived, 7-percent weight loss.
25-----	10	Capsule--	Poisoned after 9 and survived, 5-percent weight loss.
25-----	10	Drench---	Poisoned after 8 and survived, 15-percent weight loss.
50-----	199	---do-----	Poisoned after 192 and died.
50-----	10	---do-----	Poisoned and sacrificed, 19-percent weight loss.
50-----	10	Capsule--	Poisoned after 3 and survived, 23-percent weight loss.
100-----	16	Drench---	Poisoned after 3 and died.
100-----	8	Capsule--	Poisoned after 1 and died.
100-----	10	---do-----	Do.
250-----	2	Drench---	Do.
400-----	2	---do-----	Do.
<b>Chickens:<sup>3</sup></b>			
25-----	10	Capsule--	61-percent weight gain.
50-----	10	---do-----	24-percent weight gain.
100-----	10	---do-----	20-percent weight gain.
250-----	10	---do-----	2-percent weight loss.
Controls-----			45-percent weight gain.

TABLE 16.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloro-4,6-bis(ethylamino)-s-triazine (simazine)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
10-----	10	Drench---	NIE.
25-----	6	---do-----	Poisoned after 3 and survived, 5-percent weight loss.
25-----	10	---do-----	Poisoned and survived, 12-percent weight loss.
50-----	10	---do-----	Poisoned after 3 and survived, 21-percent weight loss, long recuperative period.
100-----	7	---do-----	Poisoned after 3 and sacrificed.
250-----	3	---do-----	Poisoned after 1 and survived, 11-percent weight loss.
<b>Sheep:</b>			
25-----	10	---do-----	NIE.
50-----	31	---do-----	Poisoned after 17, died 14 days later, 13-percent weight loss.
50-----	10	---do-----	Poisoned and survived, 18-percent weight loss.
100-----	14	---do-----	Poisoned after 4 and died.
100-----	10	Capsule--	Poisoned, with 13-percent weight loss, died 4 days after last dose.
250-----	3	Drench---	Poisoned after 1 and survived, 9-percent weight loss.
250-----	10	Capsule--	Poisoned after 3 and died.
400-----	9	Drench---	Do.
<b>Chickens:<sup>3</sup></b>			
25-----	10	Capsule--	52-percent weight gain.
50-----	10	---do-----	29-percent weight gain.
100-----	10	---do-----	20-percent weight gain.
250-----	10	---do-----	1 died after 8, 10-percent weight gain in survivors.
Controls-----			43-percent weight gain.

<sup>1</sup> Simazine, 80 percent wettable powder, Geigy Agricultural Chemicals, Ardsley, N. Y.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

<sup>1</sup> Atrazine, 80 percent wettable powder, Geigy Agricultural Chemicals, Ardsley, N. Y.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

a swollen, friable, often light-brown liver; and petechiae on the surface of the epicardium. At necropsy, one chicken had an enlarged, congested liver and congestion of the intestinal mucosa.

Application rates for simazine range from 1 to 9.6 pounds actual per acre. Rates in excess of 3 pounds per acre would be hazardous for cattle and in excess of 5 pounds for sheep. The 9.6-pound rate would be hazardous for chickens.

## 2,4-Bis(isopropylamino)-6-methoxy-s-triazine (prometone)

Both cattle and sheep were more susceptible to doses by drench than by capsule (table 17). Cattle were poisoned at 10 mg./kg., sheep at 25 mg./kg. Chickens dosed at 25 mg./kg. had a significant reduced weight gain.

Signs of poisoning in cattle and sheep were anorexia and diarrhea, with increased salivation. At necropsy the sheep dosed at 100 mg./kg. had petechiae on the surface of the abomasal mucosa and areas of hemorrhage in the small intestine. The liver was swollen and friable and the kidneys were congested.

Application rates for prometone for use on noncrop areas vary from 9.5 to 57 pounds actual per acre. Rates in excess of 1 pound are hazardous for cattle; rates of 3 pounds or greater are hazardous for sheep and chickens.

## 2-Chloro-4,6-bis(isopropylamino)-s-triazine (propazine)

Cattle dosed by drench at 50 mg./kg. showed evidence of poisoning after 2 doses, but survived 10 with significant weight loss (table 18). A yearling dosed by drench at 25 mg./kg. was poisoned after 3, whereas another dosed by capsule had no ill effects after 10. Three of the 5 sheep dosed at 25 mg./kg. by either capsule or drench were poisoned after 5 to 16. The 4th sheep tolerated 59 by capsule with no ill effect, whereas the 5th sheep lost weight initially but regained it. Chickens were poisoned at 100 mg./kg., with significant reduced weight gains.

Signs of poisoning in cattle and sheep were anorexia and increasing depression and weakness. On occasion, a stilted gait was observed. The sheep dosed at 500 mg./kg. had lost 16 percent of its weight by the time it had received 10 doses, and anorexia continued for 14 days after the 10th dose. This sheep lost a total of 28 percent of its pre-exposure weight before it died.

At necropsy on sheep, there was congestion of

the kidneys, adrenals, and liver. The mucosa of the abomasum and intestines was reddened. In sheep that died after long periods of toxicosis, there were often blood-engorged lungs, with froth in the respiratory tract. There were excessive amounts of red-tinged fluid in the thoracic and abdominal cavities. The one chicken fatality had congestion of the kidneys and the intestinal mucosa.

Application rates for propazine range from 2 to 4 pounds actual per acre. The maximum rate would be a hazard to cattle and sheep but not to chickens.

TABLE 17.—Results of multiple oral dosing of cattle, sheep, and chickens with 2,4-bis(isopropylamino)-6-methoxy-s-triazine (prometone)<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<hr/>			
Cattle:	Num-ber		
10-----	10	Capsule--	NIE.
10-----	10	Drench---	Poisoned after 8 and survived, 8-percent weight loss. <sup>3</sup>
25-----	10	---do----	Poisoned after 1 and survived, 31-percent weight loss.
50-----	5	---do----	Poisoned after 2 and survived, 6-percent weight loss.
Sheep:			
10-----	10	---do----	NIE.
25-----	10	---do----	Poisoned after 4 and survived, 9-percent weight loss.
25-----	10	Capsule--	NIE. <sup>3</sup>
50-----	10	Drench---	Poisoned after 2 and survived, 10-percent weight loss.
50-----	10	Capsule--	Poisoned after 1 and survived, 35-percent weight loss.
100-----	4	Drench---	Poisoned after 1 and died.
Chickens: <sup>4</sup>			
10-----	10	Capsule--	48-percent weight gain.
25-----	10	---do----	29-percent weight gain.
50-----	10	---do----	28-percent weight gain.
100-----	10	---do----	22-percent weight gain.
250-----	10	---do----	13-percent weight gain.
Controls-----			43-percent weight gain.

<sup>1</sup> Prometone, 25 percent emulsifiable concentrate, Geigy Agricultural Chemicals, Ardsley, N. Y.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Pneumonia developed 1 day after last dose.

<sup>4</sup> Average results of 5 treated chickens.



TABLE 18.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloro-4,6-bis(isopropyl-amino)-s-triazine (propazine)<sup>1</sup>*

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>	Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>				<b>Sheep—Con:</b>			
10-----	10	Drench---	NIE.	50-----	59	---do----	Poisoned after 8, 11-percent weight loss, died 12 days after last dose.
25-----	6	---do----	Poisoned after 3 and survived. <sup>3</sup>	50-----	59	---do----	Poisoned and survived, 22-percent weight loss.
25-----	10	Capsule--	NIE.	50-----	10	Drench---	Poisoned and survived, 13-percent weight loss.
50-----	10	Drench---	Poisoned after 2 and survived, 16-percent weight loss.	100-----	10	---do----	Poisoned and survived, 20-percent weight loss.
100-----	5	---do----	Poisoned after 1 and survived, 12-percent weight loss.	250-----	10	---do----	Poisoned after 3 and survived, 21-percent weight loss.
250-----	7	---do----	Poisoned after 2 and survived, 21-percent weight loss.	500-----	10	---do----	Poisoned after 1, 16-percent weight loss, died 14 days after last dose.
<b>Sheep:</b>				<b>Chickens: <sup>4</sup></b>			
10-----	10	Drench---	NIE.	50-----	10	Capsule--	49-percent weight gain.
25-----	10	---do----	Poisoned and survived, 5-percent weight loss.	100-----	10	---do----	28-percent weight gain.
25-----	5	Capsule--	Poisoned and died.	250-----	10	---do----	1 died after 6, 18-percent weight gain in survivors.
25-----	21	---do----	Poisoned after 16 and survived, 19-percent weight loss during trial period.	Controls-----			33-percent weight gain.
25-----	59	---do----	NIE.				
25-----	59	---do----	7-percent weight loss after 8, otherwise NIE.				
50-----	6	---do----	Poisoned after 5 and died.				
50-----	32	---do----	Poisoned after 17 and survived, 32-percent weight loss during trial period.				

<sup>1</sup> Propazine, 80 percent wettable powder, Geigy Agricultural Chemicals, Ardsley, N.Y.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Complicated by pneumonia, which was successfully treated.

<sup>4</sup> Average results of 5 treated chickens.

## 2,4-Bis[(3-methoxypropyl)amino]-6-(methylthio)-s-triazine

Cattle were dosed by either drench or capsule, sheep by drench, chickens by capsule (table 19). No signs of poisoning were observed in cattle. Signs of poisoning in sheep dosed at 100 mg./kg. were observed after 1 and 8 doses. Chickens dosed at 250 mg./kg. had reduced weight gain, and 3 dosed at 500 mg./kg. died.

Anorexia was the most prominent sign of poisoning, but diarrhea and depression were noted

at times. A swelling in the mandibular area developed suddenly in a yearling dosed at 50 mg./kg. after the 8th and final dose. This swelling was considered to be caused by the chemical irritation on the pharyngeal mucosa and resulted in dyspnea and partial anorexia. (See p. 5.) A sheep was severely poisoned at 250 mg./kg. after one dose and showed lameness and an uncoordinated gait within one-half hour after it was dosed. It became prostrate, extremely depressed, and moribund during the next 7 hours. Even though we expected the sheep to die, after a



TABLE 19.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,4-bis [(3-methoxypropyl) amino]-6-(methylthio)-s-triazine*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<i>Number</i>			
Cattle:			
25-----	10	Drench---	NIE.
50-----	8	---do-----	27-percent weight loss due to irritation effect. <sup>3</sup>
100-----	10	Capsule--	NIE.
Sheep:			
25-----	10	Drench---	Do.
50-----	10	---do-----	Do.
100-----	10	---do-----	Poisoned after 1 and survived, 12-percent weight loss.
100-----	9	---do-----	Poisoned after 8 and survived, 10-percent weight loss.
250-----	1	---do-----	Poisoned and survived, 10-percent weight loss.
Chickens: <sup>4</sup>			
100-----	10	Capsule--	40-percent weight gain.
250-----	10	---do-----	21-percent weight gain.
500-----	10	---do-----	3 died after 4 to 7, no weight change in survivors.
Controls-----			43-percent weight gain.

<sup>1</sup> Lambast®, 25.5 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

<sup>4</sup> Average results of 5 treated chickens.

period of several days of partial anorexia, it made a slow but uneventful recovery. At necropsy on three chickens dosed at 500 mg./kg., congestion of the intestinal mucosa and the kidneys was seen.

Registration of this herbicide was cancelled in 1968; however, 10 pounds actual per acre would be hazardous for sheep but not for cattle or chickens.

## 2,4-Bis(isopropylamino)-6-(methylthio)-s-triazine

Cattle and sheep were dosed by drench, with poisoning at 50 mg./kg. for one yearling after 2 doses and at 100 mg./kg. for 2 sheep after 6

and 8 (table 20). A significant reduction in weight gain occurred at 50 mg./kg. for chickens dosed by capsule.

Signs of poisoning in cattle and sheep were anorexia and depression. The severely poisoned yearling that died after 4 doses at 100 mg./kg. had an uncoordinated gait before prostration and death. The sheep given 9 doses at 100 mg./kg. had a similar uncoordinated gait.

At necropsy on one sheep, congestion of the respiratory tract mucosa and blood-engorged lungs were seen, with the subcutaneous tissue surrounding the larynx and upper trachea filled with reddish, edematous infiltrate. The liver was friable and light brown, the kidneys were congested, and the adrenals were enlarged. Lesions in the yearling were similar to those in the sheep.

Application rates for this herbicide range from 0.64 to 6 pounds actual per acre. The maximum rate would be hazardous for cattle and chickens but not for sheep.

TABLE 20.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,4-bis(isopropylamino)-6-(methylthio)-s-triazine*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<i>Number</i>			
Cattle:			
25-----	10	Drench---	NIE.
50-----	6	---do-----	Poisoned after 2 and survived, 6-percent weight loss.
100-----	4	---do-----	Poisoned after 1 and died.
Sheep:			
25-----	10	---do-----	NIE.
50-----	10	---do-----	Do.
100-----	9	---do-----	Poisoned after 8 and survived, 8-percent weight loss.
100-----	10	---do-----	Poisoned after 6 and died.
Chickens: <sup>3</sup>			
25-----	10	Capsule--	48-percent weight gain.
50-----	10	---do-----	44-percent weight gain.
100-----	10	---do-----	34-percent weight gain.
250-----	10	---do-----	Poisoned after 2, 4-percent weight loss.
Controls-----			49-percent weight gain.

<sup>1</sup> Caparol® or Prometryne®, 80 percent wettable powder, Geigy Agricultural Chemicals, Ardsley, N. Y.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

## Benzoic Acid Compounds

### 2-Methoxy-3,6-dichlorobenzoic acid (dicamba), dimethylamine salts

Cattle were poisoned at 250 mg./kg. after 2 doses by drench, whereas sheep were poisoned at 500 mg./kg. after 1 (table 21). Chickens dosed by capsule at 50 mg./kg. had significant average decreased weight gain after 10; however, those dosed at 100 mg./kg. had an average increased weight gain.

Signs of poisoning in cattle and sheep were convulsions, tympanites, and prostration. At necropsy on sheep, lymph nodes throughout the body were enlarged and hemorrhagic and there were areas of hemorrhage on the surface of the epicardium. The liver and kidneys were congested, the spleen was enlarged, and there was redness of the intestinal mucosa.

Application rates for dicamba range from 0.125 to 1 pound actual acid equivalent per acre. These rates would not be a hazard to the three test species.

TABLE 21.—Results of multiple oral dosing of cattle, sheep, and chickens with 2-methoxy-3,6-dichlorobenzoic acid (dicamba), dimethylamine salts <sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
100-----	10	Drench---	NIE.
250-----	2	---do-----	Poisoned and survived.
250-----	10	---do-----	NIE.
<b>Sheep:</b>			
100-----	10	---do-----	Do.
200-----	7	---do-----	Do.
250-----	10	---do-----	Do.
500-----	2	---do-----	Poisoned and died.
500-----	3	---do-----	Poisoned after 1 and died.
1, 000-----	1	---do-----	NIE.
<b>Chickens:<sup>3</sup></b>			
50-----	10	Capsule--	43-percent weight gain.
100-----	10	---do-----	55-percent weight gain.
250-----	10	---do-----	45-percent weight gain.
500-----	10	---do-----	49-percent weight gain.
Controls-----			53-percent weight gain.

<sup>1</sup> Banvel D®, 4 lb./gal. emulsifiable concentrate, Velsicol Chemical Corp., Chicago, Ill.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

### 2,3,6-Trichlorobenzoic acid (2,3,6-TBA) and related polychlorobenzoic acids, dimethylamine salts

Cattle dosed by drench at 500 mg./kg. were poisoned by 1 and 2 doses, with one yearling surviving 8 (table 22). Reactions of sheep drenched at different dosage levels varied, although a significant weight loss occurred at 25 mg./kg. after 10. Chickens dosed at 250 mg./kg. by pipette had a significant reduction in weight gain; in contrast, chickens dosed at 500 mg./kg. had an insignificant reduction.

Signs of poisoning in cattle and sheep usually

TABLE 22.—Results of multiple oral dosing of cattle, sheep, and chickens with 2,3,6-trichlorobenzoic acid (2,3,6-TBA) and related polychlorobenzoic acids, dimethylamine salts <sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
250-----	10	Drench---	NIE.
500-----	8	---do-----	Poisoned after 2 and survived.
500-----	1	---do-----	Poisoned and died 6½ months after dose.
<b>Sheep:</b>			
10-----	10	---do-----	NIE.
25-----	10	---do-----	5-percent weight loss.
50-----	10	---do-----	Poisoned, 15-percent weight loss, sacrificed 60 days after last dose.
50-----	10	---do-----	NIE.
100-----	10	---do-----	5-percent weight loss.
100-----	10	---do-----	NIE.
250-----	10	---do-----	Poisoned after 3, 9-percent weight loss, died 2 days after last dose.
250-----	10	---do-----	Poisoned and died 2 days after last dose, 6-percent weight loss.
<b>Chickens:<sup>3</sup></b>			
100-----	10	Pipette---	43-percent weight gain.
250-----	10	---do-----	30-percent weight gain.
500-----	10	---do-----	45-percent weight gain.
Controls-----			47-percent weight gain.

<sup>1</sup> Trysben®, 26.1 percent emulsifiable concentrate, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.



were anorexia, depression, diarrhea, and lameness. The yearling acutely poisoned after a single dose at 500 mg./kg. became chronically affected, with lameness persisting for 6½ months before death. Partial anorexia continued for 6 weeks in 1 sheep with appearances of abdominal pain while eating. The animal became weaker until prostration and a moribund condition developed. Then, 60 days after the last dose, the sheep was sacrificed.

At necropsy, the chronically affected yearling had edematous infiltration of the brisket, thoracic, and inner thigh muscles. At necropsy on sheep,

edema was found in the tissues surrounding the upper respiratory tract, in the pericardial sac, and in the peritoneal cavity. The liver was friable and enlarged and the kidneys appeared congested, with petechiae on the surface of the cortex. There was congestion of the intestinal and respiratory tract mucosa. The lungs were engorged with blood.

Registration of 2,3,6-TBA for use on croplands and rangelands was cancelled in 1968; however, rates in excess of 3 pounds actual per acre would be hazardous for sheep but would be no hazard to cattle and chickens.

## Miscellaneous Compounds

### 5-Bromo-3-sec-butyl-6-methyluracil (bromacil)

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 23). A yearling dosed at 250 mg./kg. by capsule was poisoned after one dose. One sheep dosed at 50 mg./kg. by drench was not poisoned after 10; another dosed at 50 mg./kg. by capsule was poisoned, along with weight loss. Chickens dosed at 250 mg./kg. had a significant reduction in average weight gain after 10.

Signs of poisoning in cattle and sheep were anorexia and depression, although tympanites and an uncoordinated gait were occasionally observed in some.

Application rates for bromacil range from 1.6 to 20 pounds actual per acre. Rates in excess of 5 pounds would be hazardous for sheep but a rate of 20 pounds would not be hazardous for cattle and chickens.

### 5-Bromo-3-isopropyl-6-methyluracil (isocil)

Cattle were dosed by drench, sheep by either drench or capsule, chickens by capsule (table 24). Cattle dosed at 50 mg./kg. were poisoned after 7 doses. Dosing was stopped after 9 when complications of pneumonia developed. A sheep dosed at 100 mg./kg. by drench was poisoned after 1 but survived 10, with significant weight loss; but a sheep dosed at 100 mg./kg. by capsule had no ill effects after 10. Chickens dosed at 250 mg./kg. had a reduced weight gain after 10.

Signs of poisoning in cattle and sheep were anorexia and depression, which were often accompanied by tympanites, an uncoordinated gait, and prostration. Convulsions were observed before death.

At necropsy enlarged, hemorrhagic lymph nodes were found in cattle and sheep. There were hemorrhages on the surface of the epicardium and lungs were congested. The upper respiratory tract mucosa was reddened. In one animal the

intestinal mucosa was congested; in another, petechiae on the surfaces of the liver and kidneys were present. At necropsy, an enlarged and congested liver, capsular hemorrhages in the spleen, and swollen, congested kidneys were seen in the chicken.

TABLE 23.—Results of multiple oral dosing of cattle, sheep, and chickens with 5-bromo-3-sec-butyl-6-methyluracil (bromacil)<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
100-----	10	Drench---	NIE.
100-----	10	Capsule--	Do.
250-----	10	---do----	Poisoned after 1 and survived, 14-percent weight loss.
<b>Sheep:</b>			
25-----	10	Drench---	NIE.
50-----	10	Capsule--	Poisoned and survived, 8-percent weight loss.
50-----	10	Drench---	NIE.
100-----	10	Capsule--	Do.
100-----	10	Drench---	Poisoned and survived, 9-percent weight loss.
250-----	5	---do----	Poisoned after 3 and survived, 9-percent weight loss.
250-----	10	Capsule--	Poisoned after 8 and survived, 8-percent weight loss.
<b>Chickens:<sup>3</sup></b>			
100-----	10	---do----	49-percent weight gain.
250-----	10	---do----	39-percent weight gain.
500-----	10	---do----	24-percent weight gain.
Controls-----			48-percent weight gain.

<sup>1</sup> Hyvar X®, 80 percent wettable powder, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

TABLE 24.—*Results of multiple oral dosing of cattle, sheep, and chickens with 5-bromo-3-isopropyl-6-methyluracil (isocil)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
25-----	10	Drench---	NIE.
50-----	9	---do-----	Poisoned after 7, 11-percent weight loss. <sup>3</sup>
100-----	10	---do-----	6-percent weight loss.
250-----	2	---do-----	Poisoned and died.
<b>Sheep:</b>			
50-----	10	---do-----	NIE.
100-----	10	---do-----	Poisoned after 1 and survived, 15-percent weight loss.
100-----	10	Capsule--	NIE.
100-----	10	Drench---	Poisoned and survived, 15-percent weight loss.
250-----	4	---do-----	Poisoned after 1 and died.
250-----	3	Capsule--	Poisoned and died.
<b>Chickens:<sup>4</sup></b>			
100-----	10	---do-----	49-percent weight gain.
250-----	10	---do-----	38-percent weight gain.
500-----	10	---do-----	1 died after 7, 12-percent weight gain in survivors.
Controls-----			47-percent weight gain.

<sup>1</sup> Hyvar Isocil®, 80 percent wettable powder, E. I. DuPont de Nemours and Co., Wilmington, Del.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Toxicity complicated by pneumonia, which developed during treatment.

<sup>4</sup> Average results of 5 treated chickens.

Application rates for isocil to noncrop areas range from 1.6 to 26 pounds actual per acre. Rates in excess of 5 pounds actual per acre would be hazardous for cattle and 10 pounds for sheep; however, even the maximum rate (26 pounds) would not be hazardous for chickens.

### Polychlorobicyclopentadiene isomers

Cattle and sheep were dosed by capsule or drench, chickens by capsule (table 25). A yearling was poisoned at 100 mg./kg. after 3 doses but survived; a sheep was poisoned at the same rate after 7 but eventually died. Chickens dosed at

TABLE 25.—*Results of multiple oral dosing of cattle, sheep, and chickens with polychlorobicyclopentadiene isomers*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
25 <sup>3</sup> -----	10	Capsule--	NIE.
50 <sup>3</sup> -----	10	---do-----	Do.
100-----	10	---do-----	Poisoned after 3 and survived, 6-percent weight loss.
250-----	3	Drench---	Poisoned after 2 and died 8 days after last dose.
<b>Sheep:</b>			
25 <sup>3</sup> -----	10	Capsule--	NIE.
50 <sup>3</sup> -----	10	---do-----	Do.
100-----	10	---do-----	Poisoned after 7, with 13-percent weight loss; died 13 days after last dose, with 34-percent weight loss.
200-----	1	Drench---	NIE.
250-----	3	---do-----	Poisoned after 1 and survived.
1,000-----	1	---do-----	Poisoned and died.
<b>Chickens:<sup>4</sup></b>			
25 <sup>3</sup> -----	10	Capsule--	40-percent weight gain.
50-----	10	---do-----	27-percent weight gain.
100-----	10	---do-----	1 died after 10, 11-percent weight loss in survivors.
250-----	9	---do-----	Affected after 3 and died after 7 to 9.
Controls-----			40-percent weight gain.

<sup>1</sup> Bandane®, 4 lb./gal. emulsifiable concentrate, Velsicol Chemical Corp., Chicago, Ill.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Technical material was used in more recent trials.

<sup>4</sup> Average results of 5 treated chickens.

50 mg./kg. showed significant weight gain reduction.

Signs of poisoning were anorexia, depression, muscular tremors, and hyperexcitability. In the sheep chronically poisoned at 100 mg./kg., there was an uncoordinated gait, followed by prostration, convulsions, and death.

At necropsy on cattle and sheep, hemorrhages were found along the brain stem and in the anterior



region of the cerebrum. Meningeal vessels were congested. The liver was friable and congested. Petechiae were seen on the surface of the epicardium. At necropsy on the chronically poisoned sheep, the lungs and the respiratory tract mucosa were congested. The liver was enlarged and friable, the kidneys were reduced in size, and the pancreas was congested. Chickens poisoned had swollen, congested livers and kidneys, and the intestinal mucosa was hemorrhagic.

Application rates for polychlorobicyclopentadiene isomers to noncrop areas, such as lawns and turf, range from 30 to 40 pounds actual per acre. These rates would be highly hazardous for all three test species.

TABLE 26.—*Results of multiple oral dosing of cattle, sheep, and chickens with 3',4'-dichloropropionanilide (propanil)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
50-----	10	Drench---	NIE.
100-----	10	---do-----	Do.
250-----	1	---do-----	Poisoned and survived.
<b>Sheep:</b>			
25-----	10	---do-----	NIE.
25-----	10	Capsule--	Do.
50-----	10	Drench---	Do.
100-----	10	---do-----	Poisoned and survived, 11-percent weight loss.
100-----	10	Capsule--	NIE.
250-----	1	Drench---	Poisoned and survived, 14-percent weight loss.
<b>Chickens:<sup>3</sup></b>			
10-----	10	Capsule--	48-percent weight gain.
25-----	10	---do-----	19-percent weight gain.
50-----	10	---do-----	20-percent weight gain.
100-----	10	---do-----	3 died after 8 or 9, 13-percent weight gain in survivors.
250-----	6	---do-----	All poisoned and died after 2 to 6.
Controls-----			48-percent weight gain.

<sup>1</sup> Rogue®, 46 percent emulsifiable concentrate, Monsanto Chemical Co., St. Louis, Mo.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

### 3',4'-Dichloropropionanilide (propanil)

A yearling was poisoned at 250 mg./kg. after 1 dose by drench (table 26). One sheep was poisoned at 100 mg./kg. after 10 by drench, but another had no ill effects after 10 by capsule. Chickens dosed at 25 mg./kg. 10 times had a significant reduction in weight gain.

In cattle and sheep, the signs of poisoning at 250 mg./kg. were anorexia, depression, an uncoordinated gait, and prostration; all were observed over a period of a few hours in the 2 animals receiving 1 dose each. Anorexia was the only sign in the sheep less acutely poisoned at 100 mg./kg.

At necropsy, chickens had congested intestinal mucosa, swollen kidneys, and a distended gall bladder.

The application rate for propanil to rice crops is 6 pounds actual per acre but not to exceed 8 pounds per season. Such rates would not be a hazard to cattle and sheep, but would be to chickens.

### 2,6-Dichlorobenzonitrile (dichlobenil)

A yearling dosed at 50 mg./kg. by capsule was poisoned after 1 dose (table 27). A sheep dosed at 10 mg./kg. by capsule had no ill effects after 60. A sheep dosed at 25 mg./kg. by capsule was poisoned after 4; a sheep dosed by drench was poisoned after 10. Chickens dosed at 25 mg./kg. by capsule had significant reduced weight gains.

Signs of toxicosis in cattle and sheep were increased salivation, anorexia, and depression. Convulsions were observed before death in some instances.

At necropsy lesions in cattle and sheep were extensive as in generalized toxemia. There were swollen, hemorrhagic lymph nodes throughout the body and hemorrhages in the muscles, chiefly in the thoracic and cervical areas. Petechiae were on the surface of the epicardium. Congestion of the lungs and upper respiratory tract mucosa were commonly seen. The liver was swollen and congested in cases of acute poisoning, but often light brown and friable in prolonged or chronic poisoning. The kidneys were congested and swollen; however, in the sheep that died 30 days after the last dose, they were firm and reduced in size. The mucosa of the abomasum and of the intestinal tract was congested, whereas the mucosae of the more acutely poisoned sheep were markedly inflamed. At necropsy, chickens were notably emaciated, and

TABLE 27.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,6-dichlorobenzonitrile (dichlobenil)*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
10-----	10	Capsule--	NIE.
25-----	10	---do-----	Do.
50-----	2	---do-----	Poisoned after 1 and died.
<b>Sheep:</b>			
5-----	60	---do-----	NIE.
10-----	60	---do-----	Do.
10-----	10	Drench---	Do.
25-----	10	Capsule--	Poisoned and survived, 18-percent weight loss.
25-----	13	---do-----	Poisoned after 4 and died, 29-percent weight loss.
25-----	10	Drench---	Poisoned after 10, 15-percent weight loss, died 20 days after last dose.
50-----	10	Capsule--	Poisoned after 10, 26-percent weight loss, died 2 days after last dose.
50-----	10	Drench---	Poisoned after 6 and died, 14-percent weight loss.
100-----	1	---do-----	Poisoned and died.
<b>Chickens:<sup>3</sup></b>			
10-----	10	Capsule--	62-percent weight gain.
25-----	10	---do-----	11-percent weight gain.
50-----	10	---do-----	9-percent weight gain.
100-----	10	---do-----	2 died, 23-percent weight loss in survivors.
Controls-----			37-percent weight gain.

<sup>1</sup> Casoron®, 50 percent wettable powder, Thompson-Hayward Chemical Co., Kansas City, Kans.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

the liver, kidneys, and intestinal mucosa were congested.

Application rates for dichlobenil range from 2 to 6 pounds actual per cropland acre and 15 pounds actual per water acre. A 3-pound rate per acre would be hazardous for sheep and chickens and a 6-pound rate for cattle.

#### 4-Amino-3,5,6-trichloropicolinic acid (picloram), potassium salt

Cattle dosed at 500 mg./kg. by drench were poisoned after 8 doses; sheep dosed at 250 mg./kg. by either drench or capsule were poisoned after 9 or 10 (table 28). Chickens dosed at 500 mg./kg. had a significant reduction in average weight gain.

In cattle and sheep, weakness, depression, and anorexia were the most prominent signs of poisoning. A delayed toxicity led to the death of a yearling and a sheep 6 days after the last dose.

At necropsy on the yearling and the sheep, lymph nodes of the head, neck, and thoracic cavity were swollen and hemorrhagic. The lungs and the respiratory tract mucosa were congested.

TABLE 28.—*Results of multiple oral dosing of cattle, sheep, and chickens with 4-amino-3,5,6-trichloropicolinic acid (picloram), potassium salt*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
<b>Cattle:</b>			
100-----	10	Drench---	NIE.
250-----	10	---do-----	Do.
500-----	8	---do-----	Poisoned after 8 and died 6 days after last dose, 24-percent weight loss.
<b>Sheep:</b>			
100-----	10	Capsule--	NIE.
100-----	10	Drench---	Do.
250-----	10	Capsule--	Poisoned after 9 and died 6 days after last dose.
250-----	10	Drench---	Poisoned and survived, 6-percent weight loss.
250-----	10	---do-----	NIE.
500-----	10	---do-----	Poisoned after 2 and survived, 17-percent weight loss.
<b>Chickens:<sup>3</sup></b>			
100-----	10	Pipette---	34-percent weight gain.
250-----	10	---do-----	35-percent weight gain.
500-----	10	---do-----	32-percent weight gain.
Controls-----			38-percent weight gain.

<sup>1</sup> Tordon®, 24.9 percent emulsifiable concentrate Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Average results of 5 treated chickens.

The rumens were filled with undigested feed and livers were engorged with blood and swollen. The adrenals were enlarged and congested. The yearling had pleural adhesions and a congested pancreas. The sheep had hemorrhages throughout the heart and blood-tinged fluid in the pericardial sac. The kidneys and the intestinal mucosa of the sheep were congested.

Registration of picloram for use on cropland was cancelled in 1968; however, a rate in excess of 25 pounds actual per acre would present a hazard to sheep but not to cattle or chickens.

### 2,2-Dichloropropionic acid (dalapon), sodium salt

Cattle and sheep were dosed by either drench or capsule, chickens by capsule (table 29). A yearling dosed at 500 mg./kg. by capsule was not poisoned after 10 doses; however, a yearling dosed at 500 mg./kg. by drench, although not poisoned, developed a swelling in the parotid area after 9 days. This swelling was considered to be caused by chemical irritation of the pharyngeal mucosa. (See p. 5.) Sheep dosed at 500 mg./kg. by either drench or capsule were poisoned. One sheep dosed at 100 mg./kg. by capsule was poisoned and had a 6-percent weight loss after 10. Another sheep dosed at 100 mg./kg. by capsule 481 times had a 10-percent weight loss after 86 but suffered no ill effects. A sheep dosed at 100 mg./kg. by drench had no ill effects after 10. Chickens dosed at 250 mg./kg. had a significant average reduced weight gain after 10; whereas chickens dosed at 500 mg./kg. had slightly less reduced weight gain than the chickens dosed at 250 mg./kg.

Anorexia and depression were the signs of poisoning in the sheep. Recovery was uneventful after the dosing regimen was completed.

Application rates for dalapon range from 1.1 to 14.8 pounds actual per acre. These rates would be no hazard to the cattle and chickens, but a rate in excess of 10 pounds would be a hazard to sheep.

TABLE 29.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,2-dichloropropionic acid (dalapon), sodium salt*<sup>1</sup>

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks <sup>2</sup>
	Num-ber		
Cattle:			
250-----	10	Drench---	NIE.
500-----	9	---do-----	Irritation effect after 9. <sup>3</sup>
500-----	10	Capsule--	NIE.
Sheep:			
50-----	10	Drench---	NIE.
100-----	10	Capsule--	Poisoned and survived, 6-percent weight loss.
100-----	481	---do-----	10-percent weight loss after 86, otherwise NIE.
100-----	10	Drench---	NIE.
250-----	10	---do-----	Do.
500-----	10	---do-----	Poisoned and survived, 17-percent weight loss.
500-----	10	Capsule--	Poisoned after 7 and survived, 6-percent weight loss.
Chickens: <sup>4</sup>			
100-----	10	---do-----	43-percent weight gain.
250-----	10	---do-----	27-percent weight gain.
500-----	10	---do-----	30-percent weight gain.
Controls-----			42-percent weight gain.

<sup>1</sup> Dowpon Grass Killer®, 85 percent wettable powder, Dow Chemical Co., Midland, Mich.

<sup>2</sup> NIE indicates no ill effects apparent.

<sup>3</sup> Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in parotid area enlargement accompanied by partial anorexia and dyspnea.

<sup>4</sup> Average results of 5 treated chickens.

## COMMENT

These data have been abstracted in table 30, "Summary of dosages of various organic herbicides that cause significant weight loss, reduced weight gain, or poisoning in cattle, sheep, and chickens."



TABLE 30.—*Summary of dosages of various organic herbicides that cause significant weight loss, reduced weight gain, or poisoning in cattle, sheep, and chickens*<sup>1</sup>

Herbicide	Dosage rate			Least number of dosages for—		
		Cattle	Sheep	Chickens		
<i>Mg./kg.</i>						
Chlorophenoxy compounds:						
2,4-Dichlorophenoxyacetic acid (2,4-D), alkanolamine salts (of the ethanol and isopropanol series).	{ 500 250 200 100	{ 1 25 86	{ 7 10 8	{ 10 10 —		
2,4-Dichlorophenoxyacetic acid (2,4-D), propylene glycol butyl ether ester.	{ 250 100	{ 3	{ 2	{ 4 10		
2,4,5-Trichlorophenoxyacetic acid (2,4,5-T), propylene glycol butyl ether ester.	{ 500 250 100	{ 4	{ 4 3	{ 5 10 —		
2-(2,4,5-Trichlorophenoxy)-propionic acid (silvex), propylene glycol butyl ether ester.	{ 250 100	{ 19	{ 5 9	{ 10 10		
2-Methyl-4-chlorophenoxyacetic acid (MCPA), alkanolamine salts (of the ethanol and isopropanol series).	{ 500 250 100	{ 8	{ 6 4	{ 1 10 —		
Amide compounds:						
N,N-Dimethyl-2,2-diphenylacetamide (diphenamid).	{ 500 250 100	{ 3	{ 7	{ 10 10		
2-Chloro-N,N-diallylacetamide (CDAA).	{ 50 25	{ 1 1	{ 1 4	{ 1 10 1		
2-Chloro-N,N-diallylacetamide (CDAA) and trichlorobenzyl chloride (TCBC).	{ 250 100 50 25	{ 1 2	{ 1 2 5	{ 1 10 —		
<i>Mg./kg.</i>						
Phenyl urea compounds:						
3-(p-Chlorophenyl)-1,1-dimethylurea (monuron).	{ 500 250 100 50 25	{ 1	{ 2 4	{ 6 10 10		
3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea (linuron).	{ 250 100 50 25	{ 6 10	{ 3 4 1	{ 8 10 10		
3-Phenyl-1,1-dimethylurea (fenuron).	{ 500 250 100 250 100	{ 2	{ 3 10 8	{ 10 — —		
3-(3,4-Dichlorophenyl)-1,1-dimethylurea (diuron).	{ 50 25 10	{ 10 — —	{ 2 — —	{ 10 10 10		
Thiocarbamate compounds:						
S-2,3-Dichloroallyl diisopropylthiocarbamate (diallate).	{ 250 175 150 125 100	{ — — — —	{ 1 — — —	{ 7 10 10 10		
S-2,3,3-Trichloroallyl diisopropylthiocarbamate (triallate).	{ 50 25 250 200 175 100 50 25	{ 3 1 — — — 3 5	{ 3 1 2 — — — — —	{ — — — 10 10 — — —		

Triazine compounds:			Benzoic acid compounds:		
2-Chloro-4-ethylamino-6-isopropylamino-s-triazine (atrazine).	400	1	2-Methoxy-3,6-dichlorobenzoic acid (dicamba), dimethylamine salts.	500	1
	250	1		250	2
	100	1		50	---
	50	1		500	1
	25	2		250	---
2-Chloro-4,6-bis(ethylamino)-s-triazine (simazine).	10	8	2,3,6-Trichlorobenzoic acid (2,3,6-TBA) and related polychlorobenzoic acids, dimethylamine salts.	100	3
	5	10		50	10
	400	3		25	---
	250	1		---	---
	100	3		---	---
2,4-Bis(isopropylamino)-6-methoxy-s-triazine (prometon).	50	10	Miscellaneous compounds:	500	---
	25	1		250	1
	10	4		100	3
	500	8		50	10
	250	1		---	---
2-Chloro-4,6-bis(isopropylamino)-s-triazine (propazine).	100	1	5-Bromo-3-isopropyl-6-methyluracil (isocil).	500	---
	50	1		250	2
	25	1		100	10
	10	8		50	7
	500	1		---	---
2,4-Bis[3-methoxypropyl)-amino]-6-(methylthio)-s-triazine. <sup>2</sup>	250	2	Polychlorobicyclopentadiene isomers.	1,000	---
	100	1		250	2
	50	2		100	3
	25	3		50	---
	500	5		250	1
2,4-Bis(isopropylamino)-6-(methylthio)-s-triazine.	4	4	3',4'-Dichloropropionanilide (propanil).	100	10
	250	1		50	---
	100	1		25	---
	250	1		100	1
	100	6		50	6
	50	2	2,6-Dichlorobenzonitrile (dichlobenil).	25	4
	---	---		---	---
	---	---		500	2
	---	---		250	9
	---	---		---	---
	---	---	4-Amino-3,5,6-trichloropicolinic acid (picloram), potassium salt.	500	---
	---	---		250	---
	---	---		---	---
	---	---		500	7
	---	---		250	10
	---	---	2,2-Dichloropropionic acid (dalapon), sodium salt. <sup>2</sup>	100	---
	---	---		---	---
	---	---		---	---
	---	---		---	---
	---	---		---	---

<sup>1</sup> Broken lines indicate that either the herbicide was not tested at that rate or the herbicide was not toxic to the animal at that rate.

<sup>2</sup> No toxic dosages found for cattle.



## SUMMARY AND CONCLUSIONS

Results of studies of the toxicity of 29 organic herbicides to cattle, sheep, and chickens have been presented. A total of 126 yearling cattle, 190 one-to two-year-old sheep, and 700 six-week-old chickens were studied.

Repeated doses of the herbicides were administered in gelatin capsules or as water-diluted solutions by drench or in pipettes. The usual period of study was 10 days, or until toxicologic effects appeared. However, in a number of instances, longer and shorter term studies were made.

The signs of poisoning by most of the herbicides included anorexia and reduced weight gains. In

many instances digestion in the rumen seemed to have been impaired. Macroscopic lesions were somewhat variable and nonspecific. The liver and the kidneys were most frequently involved.

An arbitrary yield of forage and rate of consumption were selected to evaluate the hazard for cattle, sheep, and chickens likely to exist under most severe conditions of use.

The most common rates of application of many of these herbicide formulations are not a hazard to cattle, sheep, or chickens. The maximum rates of application of some approach or surpass a hazardous level in one or more of the test species.

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